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DEPARTMENT OF BIOLOGY

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Dr. Joshua Lederberg
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Dear Josh:

Thanks very much for passing along references from the seminal-title searches. I appreciate them and hope the long delay in my response has not led you to think otherwise. This is the quarter I teach my Introductory Neurobiology course, and it leaves little time for correspondence.

I had already come across the paper on neuron shape/function correlations in the visual cortex but had not heard of the one on DRG neuron cultures which was, of course, of immediate interest (though rather disappointing once in hand). Additional data from the visual cortex study was reported at the Neuroscience Society meetings in San Diego last November; I've enclosed an abstract of the report. The new data makes the correlation between structure and function, at least as revealed by the chosen classification parameters, less absolute than was suggested by the original paper.

To answer one of your questions, my own thoughts about neuron shapes and shape changes are primitive and hardly worth relaying. For immediate working purposes, in fact, they amount to little more than a tacit assumption that shape can't be irrelevant, a sense that one ought to keep alert for examples of neuron shape changes in cultures, and a continuing concern about being fooled by or missing the significance of "artifactual" neuron shapes developed as a consequence of the culture environment.

To answer another of your questions, we haven't gotten around to anything that could be called a "teaching experiment" or to attempts at controlled induction of shape changes by cell contact or otherwise. But we may have turned up one example of cell contact influence on neuron shape just by simple observation of "dirty" (not purely neuronal) cultures. Specifically, in our cultures of dispersed cells from chick

embryo spinal cords, the general appearance and particularly the extent of process arborization of the cells we think are neurons varies dramatically depending on whether the "neurons" are growing on a substrate of bare collagen or on a bed of (usually confluent) nonneuronal cells. The enclosed photos, produced by an undergraduate named Ellen Smith, will give you some idea of the differences. The neurons on bare collagen have rounded cell bodies, a few (usually only one or two) rather short, thick processes (dendrites?) and one very much longer, thin process (axon?). Neurons on beds of nonneuronal cells, on the other hand generally have flattened cell bodies with more, and more highly branched, processes (with the exception that one process--the axon?--can sometimes be seen that is relatively unbranched and extends further from the cell body than the others).

Because the cultures are only relatively dirty, that is not thoroughly overwhelmed by nonneuronal cells, both types of neuron shape can often be seen in the same culture dish. Also, because the nonneuronal cells multiply and migrate in the cultures, one can ask whether individual neurons change their appearance as their local environment is invaded by nonneuronal cells. That is the question I had Ellen working on, hoping that a clear answer would exclude the alternative proposition that the different morphologies always represent merely different types of neurons selected for survival (from the mixed spinal population) by the different substrates. Ellen claimed she did see individual cells go through the shape change, but I'm waiting for a photo-documented case before believing it. If it does turn out that contact with nonneuronal cells can induce so dramatic a morphological transformation, we'll next try to find out whether the nonneuronal cells must come from nervous tissue or whether any randomly chosen nonneuronal cells (e.g., cells from one of the popular mammalian cell lines being propagated *in vitro*) can do the trick. Then, maybe, we'll also see whether any of several simple treatments (e.g., UV irradiation to the point of genetic, but not individual, death or mild trypsinization) can rob the nonneuronal cells of their neuron altering powers.

I don't have any other examples of cell-contact mediated phenomena to report from the cultures yet, and I certainly haven't developed the systems to a stage permitting search for morphological changes that might attend cellular experiences of the subtlety suggested by the idea that shape provides a rich medium for information storage. I am curious about what your note intended by the term "intracellular" contacts. I would refer to contacts of the sort apparently involved in our spinal cord case as intercellular, but I can imagine, for example, models for control

of dendritic ramification that involve contacts between branches of processes from one and the same cell. Is that the sort of thing you had in mind?

Keep me posted on your thoughts concerning nerve cells and, if other interesting titles turn up in the searches, do send them along.

Larry

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Enclosures

P.S. It looks as though my promotion here will come through. Dave Wolstenholme says that a file of very nice letters from people outside the university, including one from you, tipped the balance. Many thanks for your contribution. L.

19.5 ANALYSIS OF MOTION SELECTIVITY IN VISUAL CORTEX NEURONS OF THE CAT. Leo Ganz* and Arthur F. Lange* (SPON: K. H. Pribram). Stanford Univ., Stanford, CA. 94305.

Moving edges of varying velocity and contrast and gratings of varying velocity and spatial frequency were employed to analyze the receptive field properties of visual cortex neurons, recorded using an extracellular microelectrode. We examined particularly how these properties changed during dark adaptation. (1) We found neurons which were selective with respect to velocity and motion direction of stimuli in the visual field, (2) The peak of the velocity function, relating rate of cell firing to the velocity of the moving stimulus, shifts in the direction of slower velocities during dark adaptation. This shift reflects, we believe, the shift in temporal properties of the retina during dark adaptation, (3) Gratings of lower spatial frequency (wider stripes) yield velocity functions that peak at proportionately faster velocities, in the same neuron, (4) Bimodal velocity functions are often obtained, suggesting the motion-sensitive cell is being activated by a temporal wave having a sequence of excitation-inhibition-excitation. These findings parallel the perception of motion by human subjects; some of these parallels will be discussed.

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19.6 STRUCTURAL AND FUNCTIONAL PROPERTIES OF INDIVIDUAL NEURONS IN THE STRIATE CORTEX OF THE CAT. J. P. Kelly* and D. C. Van Essen* (SPON: T.N. Wiesel). Dept. Neurobiol., Harvard Med. Sch., Boston, Mass. 02115

Most neurons in the striate cortex of the cat can be classified as stellate or pyramidal on morphological grounds and as simple, complex, or hypercomplex on the basis of their responses to visual stimuli. We have used the technique of intracellular dye injection to study the relationship between the anatomy and physiology of these cells. Microelectrodes filled with Procion yellow were used to stain single neurons whose receptive fields were mapped with spots and slits of light. Forty-eight cells have been successfully injected and identified. Most of the simple units were stellate (8 of 13), while pyramidal cells constituted the majority of complex cells (19 of 28) and hypercomplex cells (5 of 7). One cell with intermediate functional properties was pyramidal. Several of the injected complex cells were neither stellate nor pyramidal, but belonged to more infrequently occurring neuronal types such as multiform and double bouquet cells. Simple cells occurred most frequently in layer IV of the cortex, complex units were aggregated in both superficial and deep laminae, and hypercomplex cells were concentrated in layers II and III. These results indicate that there is a close correlation between the structure and function of individual neurons in the visual cortex.